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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/467,901	12/21/1999	JOOST VAN NEERVEN	02405.0190	2936

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EXAMINER

DO, PENSEE T

ART UNIT	PAPER NUMBER
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1641

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/467,901	Applicant(s) NEERVEN, JOOST VAN	
	Examiner Pensee T. Do	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

This application, 09467901, US PG Pub. No. 20010055778 , filed 12/21/1999 and having 3 RCE-type filings therein. This application claims Priority from Provisional Application 60113536, filed 12/22/1998 and claims foreign priority to PA199801709 , filed 12/22/1998.

Amendment Entry & Claims Status

The amendment filed on March 27, 2008 has been acknowledged and entered. Claims 1-6, 8-23 are pending and being examined.

Withdrawn Rejection(s)

Rejection under 112, 2nd paragraph in the previous office action for claim 15 is withdrawn herein.

Rejections under 102 and 103 in the previous office action are withdrawn herein because example 5 in Jardieu does not teach that the variant IgE antibodies tested are anti-IgE antibodies that could bind to the labeled normal IgE (which is indicated as the equivalent free-dissolved ligand of the present invention).

Claimed Invention

1. (Previously Presented) A method of detecting and/or quantifying an IgE antibody specific to a ligand in the form of an antigen, an antibody, or a hapten in a liquid sample suspected to contain the IgE antibody comprising the steps of:

(a) contacting (i) the sample with (ii) a free dissolved ligand in the form of an

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antigen, an antibody, or a hapten to form a mixture I comprising complexes that comprise the IgE antibody and the ligand (IgE-containing complexes),

(b) mixing the mixture I with a carrier to which is bound (iii) an IgE receptor, wherein said IgE receptor is CD23 (FcERII), to form a mixture II comprising carrier-bound IgE-containing complexes,

(c) separating the carrier-bound IgE-containing complexes from the mixture II, and

(d) determining the amount of the carrier-bound IgE-containing complexes formed by detecting a label present in the carrier-bound IgE-containing complexes, wherein the label to be detected is associated with the ligand or the IgE antibody and wherein the label to be detected is added to the complexes present in steps (a), (b), or (c) and does not form part of the carrier.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 8-16, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansen et al. (US 6,087,188) further in view of Jardieu (US 6,037,453) and Frank et al. (US 6,060,326).

Johansen et al. teach a method of detecting an antibody in a sample using a labeling compound and comprising the steps of mixing the ligand antigen, antibody or hapten bound to biotin with the sample; an antibody is directed against the antibody to be detected bound to a paramagnetic particles; and a chemiluminescent acridinium compound bound to avidin or streptavidin to form a solid phase complex; separating the solid phase from the liquid phase; and analyzing the separated solid phase for the presence of chemiluminescent complex. There are several embodiments. In one embodiment, the method comprises the following steps: mixing the ligand antigen, antibody or hapten bound to biotin or a functional derivative thereof with the sample and the antibody directed against the antibody to be detected bound to paramagnetic particles to form a first solid phase complex; adding a chemiluminescent acridinium compound covalently bound to avidin, streptavidin or a functional derivative thereof to form a second solid phase complex; magnetically separating the solid phase from the liquid phase; initiating the chemiluminescent reaction, and analyzing the separated solid phase for the presence of the chemiluminescent complex. Johansen et al. also teaches the method for the quantification of specific antibodies, such as immunoglobulins, wherein a truly parallel reference immunoassay using an identical protocol as a reference. The method comprises measuring the concentration and/or the relative contents of a specific antibody in a liquid sample, wherein the measured light emission of a separated solid phase comprising a captured specific antibody coupled to a chemiluminescent label is compared with the measured light emission obtained in a parallel reference immunoassay wherein the total contents of the class of antibodies in

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the sample to which said specific antibody belongs is measured. The method comprising the steps of mixing a ligand antigen, hapten towards which the specific antibody to be measured is directly bound to biotin or a functional derivative thereof; an antibody directed against the constant portion of the antibody to be measured bound to paramagnetic particles and a chemiluminescent acridinium compound bound to avidin, streptavidin or a functional derivative thereof with the sample to form a first solid phase from the liquid phase; magnetically separating the first solid phase from the liquid phase; initiating a chemiluminescent reaction and measuring the light emission of the separated first solid phase; mixing a ligand antibody directed against the class of antibodies to be measured bound to biotin or a functional derivative thereof; an antibody directed against the constant portion of the class of antibodies to be measured bound to paramagnetic particles ; and a chemiluminescent acridinium compound bound to avidin, streptavidin or a functional derivative thereof wherein the term total shall mean the entire amount of the designated class of immunoglobulins (e.g. IgA, IgE, etc.) With the sample to form a second solid phase complex, magnetically separate the second solid phase from the liquid phase; initiating the light emission of the separated first solid phase with that of the separated second solid phase. The specific antibody to be measured in the sample is preferably a specific immunoglobulin selected from the group consisting of IgA, IgD, IgE, IgG, IgM and subclasses thereof. (See col. 3, line 30-c01. 5, line 45).

However, Johansen et al. fails to teach using an IgE receptor such as CD23 (FcERII) to bind IgE antibody/ligand complexes. Johansen also fails to teach claim 15,

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wherein the IgE is quantified using CD23 alone to obtain a first measurement and using FcεRI alone to obtain a second measurement, and using both first and second measurements as the basis for evaluating the immunological status of the subject.

Jardieu teaches an assay protocol for IgE antibody variants, which comprises coating the Fc epsilon RI or RII (CD23) receptor on a well plate (carrier). In a separate plate, the sample comprising IgE variants and a reference murine MaE11 monoclonal antibody were mixed with a normal biotinylated IgE (mixture 1). The Fc epsilon RII coated well is incubated with 50 ul of the *mixture 1 (forming mixture2)*; adding a streptavidin-HRP (horse-radish peroxidase) to mixture 2. Then the plate was washed-separation step; Adding a substrate to the plate for developing a detectable color. (see col. 42, lines 1-27). The label (streptavidin-HRP) does not associate with the carrier/plate coating the Fc epsilon RII receptor because the streptavidin would bind to the biotinylated IgE (ligand). Regarding claim 15, Jardieu teaches that FcεRI and FcεRII (CD23)-specific, differential binding polypeptides are useful for diagnostics and therapeutics. (col. 23, lines 30-42). Jardieu also teaches method of identifying immunoglobulin analogues that bind FcεRI but not FcεRII- CD23). (see col. 3, lines 36-45).

Frank et al. teaches detecting IgE antibodies using a Fc epsilon receptor FcεR instead of anti-IgE antibodies to avoid cross-reactivity with other antibody idiotypes such as gamma isotypes antibodies. Frank also teaches that IgE binds to the Fc epsilon receptor with high affinity than the anti-IgE antibodies (See col. 1, line 45-col. 2, line 10).

It would have been obvious to one of ordinary skill in the art to use the IgE receptor, CD23 as taught by Jardieu in place of the anti-IgE antibody in the method of Johansen because it is well known that Fc epsilon receptor binds to the IgE with higher affinity and no cross-reactivity with other gamma isotypes antibodies as taught by Frank. Regarding claim 15, it would have been obvious to one of ordinary skills in the art to evaluate the immunological status of a subject by quantifying IgE that binds to FCEH but not to FCEL or IgE that binds to FECL but not to FCEH as taught by Jardieu. Since IgE involves in allergic conditions, and there are certain IgE that binds to FECH but not to FECL and certain IgE that binds to FECL but not to FECH, it would have been obvious to one of ordinary skills in the to quantify both types of IgE by taking both measurements of IgE that binds to the FECL and IgE that binds to FECH in order to accurately assess the allergic condition of a subject.

Claims 6, 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansen et al. (US 6,087,188) in view of Jardieu and Frank et al. (US 6,060,326), and further in view of Arnold, Jr. et al. (US 6,004,745).

Johansen et al. , Jardieu and Frank et al. have been discussed above.

However, Johansen, Jardieu and Frank fail to teach adding label after a first separation step and a second separation to separate the non-complexed labels.

Arnold, Jr. discusses in the background section that a typical sandwich assay involve incubating an immobilized antibody (IgE receptor) with a test medium (sample).

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Antigens, if in the medium, will bind to the antibody. After incubation, unbound antigen is removed in a separation step. After a second, or simultaneous incubation with a solution of labeled antibody, the bound antigen becomes sandwiched between the immobilized antibody and the labeled antibody. After a second separation step, the amount of labeled antibody can be determined as a measure of the antigen in the medium. (see col. 1, lines 55-66).

It would have been obvious to one of ordinary skill in the art to add the label molecule after a first separation step and then separating the non-complexed labels as discussed in Arnold, Jr. using the reagents in the method of Johansen modified by Jardieu and Frank because such second separation steps, although time consuming, increases the sensitivity of the assay results. Furthermore, since the non-complexed immobilized antibody and the non-complexed labels are separated one at a time, cross-reactivity between the label and the immobilized antibody/reagent is eliminated.

Response to Arguments

Applicant's arguments with respect to claims 1-6, 8-23 have been considered but are moot in view of the new ground(s) of rejection.

Applicants argue that there is no teaching in Jardieu to suggest that the variant IgE antibodies tested in example 5 are anti-IgE antibodies that could bind to the labeled normal IgE antibodies (which are the equivalent free dissolved ligand of the present invention) in the assay.

The new grounds of rejections now remedy the deficiency.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641